REMARKS

Status of the Claims

Claims 1-30 were currently pending. Claims 1-4 and 28-30 are drawn to non-elected inventions and are cancelled herein without prejudice or disclaimer. None of the claims has been amended in this response.

Entry of the amendment and reconsideration in view of the following comments is respectfully requested. With respect to all cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejection Under 35 U.S.C. § 102

Claims 5-9, 12-16, 18, 20, 22, 25 and 26 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Livesey (U.S. Pat. No. 4,865,871, hereinafter "Livesey").

The Office alleged that Livesey "discloses a kit comprising a self-contained cell culture vessel that includes a sample holder (Figure 4:100) for accommodating cell reservoirs (Figure 4:111) and media reservoirs (Figure 4:111). This is disclosed in column 17, lines 6-17. Column 15, lines 3-21 state that the sample holder is positioned within a gas reservoir (Figure 4:90) capable of being used to hold a dry nitrogen gas." (OA at pages 2-3). Applicants traverse this rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

Livesey does not teach each and every element as set forth in claim 5. Claim 5 is directed to a self-contained cell culture vessel comprising a cell reservoir, a media reservoir, and a gas reservoir; cells and a cryoprotectant disposed in said cell reservoir; a liquid cell culture medium disposed in said media reservoir in an amount capable of diluting the cryoprotectant to a volume suitable for cell growth; and gas disposed in the gas reservoir.

Livesey discloses an apparatus for the cryopreparation of tissue samples. The tissue sample can be treated with a cryoprotectant prior to vitrification in the disclosed apparatus. After vitrification, the sample is transferred via a specimen transport and fed to a specimen holder (also called a sample holder) that is maintained in a temperature-controlled container. (Col. 9, lines 33-36). The sample is then dehydrated. (Col. 9, line 49 – Col. 10, line 66). The tissue may then be further treated, i.e., by polymerization with resin, or is stored under inert conditions for later rehydration. (Col. 11, line 34 – Col. 12, line 12). Livesey describes the apparatus used for such processes in Columns 12 – 18.

Livesey does not describe a self-contained apparatus for culturing cells, but instead only describes an apparatus for *cryopreserving* cells. Livesey also does not describe a media reservoir. Livesey describes part **111** of Figure 4 as a well in the sample holder, which creates "tissue reservoirs," such that "the cryoprepared tissue samples are individually inserted into tissue reservoirs **111** with prechilled forceps as previously disclosed." (Col. 17, lines 11-17). Contrary to the Office's assertions, this tissue reservoir **111** is not analogous to a media reservoir, but is instead a *cell reservoir.* Livesey never teaches or suggests that the tissue reservoir can contain a liquid cell culture medium in an amount adapted to dilute the cryoprotectant to a volume suitable for cell growth. There is no motivation to include cell culture medium in the tissue reservoirs of Livesey since this would negate the efficacy of the cryopreservation process.

Since Livesey does not teach every limitation of the claims, it does not anticipate the pending claims. Applicants respectfully request that the rejection of claims 5-9, 12-16, 18, 20, 22, 25 and 26 under 35 U.S.C. § 102 be withdrawn.

Rejection Under 35 U.S.C. § 103

Rajotte in view of Wilson

Claims 5-10, 13, 15-18, 20, 22 and 25-27 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Rajotte (US 5863715) in view of Wilson (US 5693537).

With respect to Rajotte, the Office asserted that:

> Rajotte discloses a kit comprising a self-contained cell culture vessel comprising a cell reservoir and a media reservoir in the form of detachable pouches (Figure 6:3a) located above an internal chamber (Figure 6:4). Rajotte teaches in column 4, lines 20-60 that cells, DMSO cryoprotectant, and cell culture media are retained within the upper portions. Rajotte, however, does not indicate that a gas reservoir is provided.

The Office acknowledges that Rajotte differs from the instant claims in failing to teach a gas reservoir.

The Office asserted that Wilson teaches "a tissue flask for cell culture that comprises a culture chamber (Figure 5:40) bounded on one side by a gas permeable membrane (Figure 5:120) in communication with a gas reservoir (Figure 5:190). Column 7, lines 47-67 indicate that critical gases are moved to and from the culture chamber through the gas permeable membrane."

The Office further asserted:

> At the time of the invention, it would have been obvious to provide the Rajotte kit with an additional storage unit at the upper portion capable of serving as a gas reservoir. Prior to and following freezing, this additional reservoir would provide the cell culture with necessary critical gases required for growth and maintenance. Wilson teaches that the coupling of a gas reservoir to a cell culture compartment using a gas permeable membrane is well known in the art. Gas permeable membranes such as the one described in Wilson are formed from materials well known in the art, and could be incorporated into the Rajotte kit with only minor structural alteration.

Applicants respectfully traverse this rejection and submit that the Office has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three

criteria must be met. First, there must be some suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations. These requirements are summarized in the MPEP (MPEP §2143, and §2143.01 to §2143.03), *citing In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); and *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Even under KSR, the "key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious." MPEP § 2141.III.

Applicants respectfully submit that cited combination of references does not teach or suggest the claimed device.

Claim 5 is directed to a self-contained cell culture vessel comprising a cell reservoir, a media reservoir, and a gas reservoir; cells and a cryoprotectant disposed in said cell reservoir; a liquid cell culture medium disposed in said media reservoir in an amount capable of diluting the cryoprotectant to a volume suitable for cell growth; and gas disposed in the gas reservoir.

Rajotte teaches a method and apparatus for cryopreserving biological material. (Abstract and Col. 2, lines 46-49). The cryopreservation devices comprise a bag having two laterally spaced separate and detachable compartments that provide an auxiliary cryopreservation storage until that can be used for viability testing. (*Id.*) This bag is shown in Figure 6. Rajotte states, "the freezer bag is specifically designed to allow known volumes of the preparation of tissue to be refluxed back from the main freezer bag into the two smaller side compartments." (Col. 4, lines 43-46). The side bags are removed for further testing. (Col. 4, lines 56-58).

These side compartments are not media reservoirs that contain a liquid cell culture medium disposed therein in an amount capable of diluting the cryoprotectant to a volume suitable

for cell growth when combined with the cells and cryoprotectant from the cell reservoir. Rajotte describes the process of thawing and using the frozen cells at Col. 3:66 – Col. 4, line 4:

> When cryopreserved material is needed, it is retrieved from storage and rapidly thawed, e.g., at about 150° C. to 200° C./min 0° C., and then placed in an ice slush. The cryoprotectant is then removed either by sucrose or slow step dilution *before being transferred to isotonic media* and readied for in vitro viability testing or transplantation.

Rajotte thus explicitly describes that the cells and cryoprotectant that are transferred to the side compartment are treated to remove the cryoprotectant, and then the cells are transferred to isotonic media for further study i.e., testing, culture or transplantation. Rajotte further describes the two processes in detail in Col. 7, lines 46 – Co. 8, line 5. When sucrose dilution is used, the freezer bag is drained into a separate centrifuge tube, and centrifuged. Sucrose and media are added to the tube in aliquots. Slow step dilution involves adding media to the bag containing the cells to dilute the concentration of the cryoprotectant. The side compartments thus do not contain media for diluting the cryoprotectant. According to Rajotte, the media is separate from the side compartment/freezer bags, and is added to the bags.

Accordingly, Rajotte does not teach a self-contained cell culture vessel and does not teach a media reservoir containing a liquid cell culture medium disposed in said media reservoir in an amount capable of diluting the cryoprotectant to a volume suitable for cell growth when combined with the cells and cryoprotectant from the cell reservoir. As acknowledged by the Office, Rajotte also does not teach a gas disposed in a gas reservoir.

Wilson does not cure these deficiencies in Rajotte. Wilson teaches a tissue culture flask comprising a cell culture compartment, a basal medium compartment, and a gas reservoir that is in communication with the culture chamber. Wilson's basal medium compartment does not satisfy the current claim requirement that the apparatus contain a media reservoir containing a liquid cell culture medium disposed in said media reservoir in an amount adapted to dilute the cryoprotectant to a volume suitable for cell growth when combined with the cells and cryoprotectant from the cell reservoir. Wilson's basal medium compartment is separated from the cell culture compartment by a

selectively permeable membrane for certain classes of molecules. (Col. 3, lines 1-4). The media contained in Wilson's basal medium compartment does not combine with cells and cryoprotectant in the cell culture compartment to dilute the cryoprotectant. Wilson does not even teach that the cells in its cell reservoir can contain cryoprotectant. Since Wilson's cells do not contain cryoprotectant, there is no motivation to include a media reservoir in Wilson's device that contains a liquid cell culture medium in an amount adapted to dilute the cryoprotectant in the cell reservoir when the contents of the two reservoirs are combined.

In the absence of a teaching or suggestion of each and every claim element, the cited combination fails render obvious claim 5 (and dependent claims). Thus, the claimed devices and methods are patentable over Rajotte in view of Wilson. Since neither Rajotte nor Wilson, alone or in combination, disclose every element of claim 5, Applicants respectfully request that the rejection of claims 5-10, 13, 15-18, 20, 22 and 25-27 under 35 U.S.C. § 103 be withdrawn.

Rajotte in view of Wilson and further in view of Mullen or Anderson

Claims 11 and 24 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Rajotte in view of Wilson as applied to claims 8 and 18, and further in view of Mullen (US 5679565). Claims 19, 21 and 23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Rajotte in view of Wilson as applied to claims 18 and 20, and further in view of Anderson (US 20060246490).

With respect to Mullen, the Office asserted:

> Mullen discloses a means for storing and preserving tissues that includes an internal compartment (Figure 1:12) serviced by a channel (Figure 1:28) for conveying fluids. Mullen teaches in column 5, lines 7-22 that a cell filter (Figure 1:22) is attached to the channel.
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> At the time of the invention, it would have been obvious to provide the kit of Rajotte with a filter means at the inlet/outlet channel capable of retaining tissue cells within the kit while preventing the passage of contaminants. Filter means, as evidenced by Mullen, are considered to be well known in the cell culture art, and are beneficial because they serve to prevent contamination. The cell filter of Mullen would serve

> the additional advantage if incorporated into the Rajotte kit of maintaining stored tissue inside the reservoir, thereby preventing undesirable tissue loss during the removal of fluids.

With respect to Anderson, the Office asserted:

> Anderson discloses a substrate for measuring the presence of biochemical analytes in a sample solution. Anderson teaches in paragraph [0183] that ball valves are common means for controlling fluid motion in a channel. Anderson additionally teaches in paragraphs [0338] and [0339] that micro electro mechanical systems are likewise commonly used as valve means. . . .
>
> At the time of the invention, it would have been obvious to provide any known means for regulating fluid flow in the Rajotte device as a substitute for the mechanisms already disclosed by Rajotte. Anderson teaches that MEMS and ball valve structures are commonly implemented in microfluidic systems, and that each represents a functionally equivalent way to restrict fluid flow. Accordingly, it would have been obvious to implement these well known features in the Rajotte kit in order to predictably and effectively control the movement of fluid to and from the various reservoirs.

As described supra, neither Rajotte nor Wilson, alone or in combination, disclose every element of claim 5 (or its dependent claims). Neither of Mullen or Anderson cures this deficiency. None of these references teach or suggest a self-contained cell culture vessel nor do they teach or suggest a device having a media reservoir containing a liquid cell culture medium disposed in said media reservoir in an amount capable of diluting the cryoprotectant to a volume suitable for cell growth when combined with the cells and cryoprotectant from the cell reservoir.

Since neither Rajotte nor Wilson, alone or in combination with Mullen or Anderson disclose every element of claim 5 (or its dependent claims), Applicants respectfully request that the rejection of claims 11, 19, 21, 23, and 24 under 35 U.S.C. § 103 be withdrawn.

CONCLUSIONS

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 220002067500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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